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5,10,20,25,35,40-Hexanornonapyrrin: The Largest Structurally Characterized Oligopyrrole Prepared to Date

Pierfrancesco Morosini,[†] Markus Scherer, Sylvie Meyer, Vincent Lynch, and
Jonathan L. Sessler*

Department of Chemistry and Biochemistry, The University of Texas at Austin, Austin, Texas 78712

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The synthesis and X-ray diffraction-based characterization of a nonapyrrolic oligomer **2** [5,5″-bis((2-(ethoxycarbonyl)-3,4,3′,4′,3″,4″-hexamethyl-5,2′:5′,2″-terpyrrol-5″-yl)vinyl)-3,4,3′,4′,3″,4″-hexamethyl-2,2′:5′,2″-terpyrrole] is reported. It was prepared by condensing 2 equiv of the 2-(ethoxycarbonyl)-2″-formyl-3,4,3′,4′,3″,4″-hexamethyl-5,2′:5′,5″-terpyrrole (**8**) with 1 equiv of 3,4,3′,4′,3″,4″-hexamethyl-2,2′:5′,2″-terpyrrole (**9**). A similar procedure, involving the condensation of 1 equiv of the 2-(ethoxycarbonyl)-2″-formyl-3,4,3′,4′,3″,4″-hexamethyl-5,2′:5′,5″-terpyrrole (**8**) with 1 equiv of 2-(ethoxycarbonyl)-3,4,3′,4′,3″,4″-hexamethyl-5,2′:5′,2″-terpyrrole (**10**) was found to give rise to the corresponding hexameric system **4** bis(2-(ethoxycarbonyl)-3,4,3′,4′,3″,4″-hexamethyl-5,2′:5′,2″-terpyrrol-5″-yl)methene, a system that was likewise characterized by X-ray diffraction methods. It was also found that replacing the monoformyl terpyrrole **8** by the corresponding bipyrrole, namely 2-(ethoxycarbonyl)-2′-formyl-3,4,3′,4′-tetramethyl-5,5′-bipyrrole (**13**), and condensing 2 equiv of it with 1 equiv of **9** gives rise to the heptapyrrole 5,5″-bis((2-(ethoxycarbonyl)-3,4,3′,4′-tetramethyl-5,2′-bipyrrol-5′-yl)vinyl)-3,4,3′,4′,3″,4″-hexamethyl-2,2′:5′,2″-terpyrrole (**3**).

Introduction

Because they touch on a number of disparate areas, linear 2,5-linked oligopyrroles have been extensively studied in the past few years. Besides playing an important role as natural products in and of themselves (e.g., bile pigments, biliproteins),[1] oligopyrrolic systems have seen important application as precursors to a range of naturally occurring porphyrins and porphyrinoids (including chlorins and corrins)[1] and as model compounds and/or starting materials in a host of biosynthetic studies.[2] In areas of less immediate biological relevance, oligopyrroles have also been studied for their interesting light-absorbing properties[3] and as nonlinear optic materials.[4] They have also been used in the construction of conducting polymers[5−7] and for the synthesis of various expanded porphyrins, all of which are of a purely abiotic origin.[8]

Inspired by this wide range of applications, we have become interested of late in developing useful syntheses of new oligopyrroles.[8b,9] Because of their connection to expanded porphyrins, we have become particularly concerned with the problem of preparing 2,5-linked oligopyrroles of extended length. While considerable effort has been devoted to this challenge, with at least several groups reporting the isolation of directly linked N-substituted oligopyrroles ($R = CH_3$, *t*-Boc) containing 10−20 subunits in decent purity (i.e., 90−95%),[5−7,10] currently

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[†] On leave from Bracco S.p.A. (via Egidio Folli 50, 20134, Milan, Italy).

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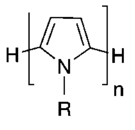
heptamer **1** ($n = 7$, R = H) appears to be the longest 2,5-linked acyclic oligopyrrole to be isolated in pure molecular form.[5,6] The question thus arises as to whether acyclic oligopyrroles of different structure but comparable length are synthetically accessible and whether they may be prepared in pure, deprotected, and air-stable form. Here, by way of answer, we report the synthesis and single-crystal X-ray structure of the oligomeric nonapyrrole **2**. We also describe the synthesis of two smaller congeneric systems, namely the linear hepta- and hexapyrroles **3** and **4**, the second of which has also been characterized by X-ray diffraction analysis. These new systems are as large (**4**) or larger (**2** and **3**) than the largest structurally characterized oligopyrrole hitherto reported (**5**).[8b]



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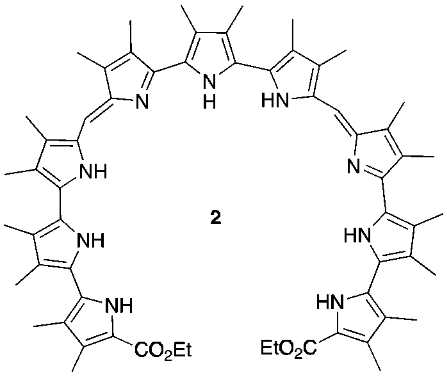

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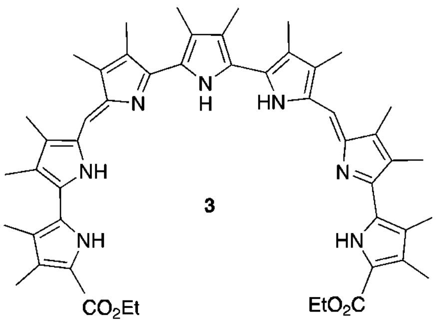

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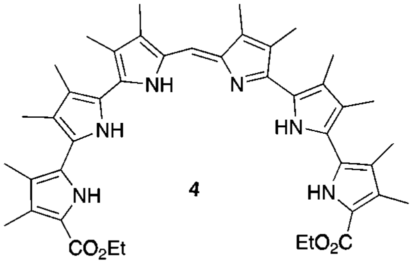

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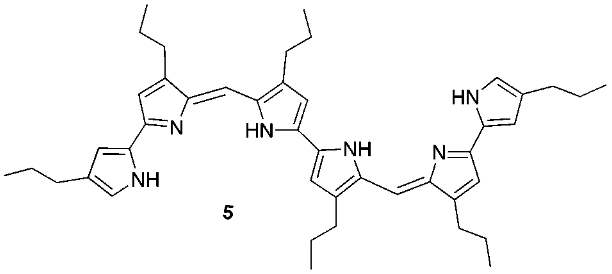

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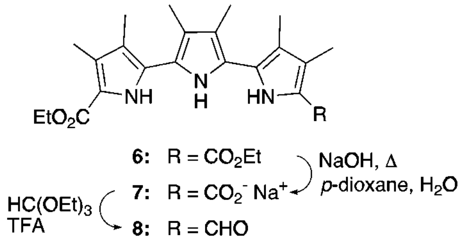
Results and Discussion

The key precursor required for the synthesis of **2** is the monoformylterpyrrole **8**. It was synthesized from the known terpyrrole diethyl ester **6**[11] shown in Scheme 1.

Scheme 1



Briefly, this monosaponification−formylation procedure involved first treating **6** with sodium hydroxide at 75 °C in a mixture of *p*-dioxane and water. Following flash column-chromatographic purification of the reaction mixture (silica gel, CH_2Cl_2/MeOH/NH_4OH (25%, aqueous), 85/15/2, v/v/v, eluent), the sodium salt of the terpyrrole monoacid[12] **7** is recovered in yields on the order of 30% (along with about 40% of the starting material **6**). Clezy formylation[13] of this intermediate then affords the requisite monoformylterpyrrole **8** in 65% yield after flash column-chromatographic purification (silica gel, $CHCl_3$ eluent).

Once **8** was in hand, the synthesis of target **2** proved straightforward. Specifically, as detailed in Scheme 2, the acid-catalyzed condensation between 2 equiv of **8** and 1 equiv of **9** in anhydrous methanol was found to give, after chromatographic purification on silica gel (NH_3-saturated hexanes/CH_2Cl_2, 75:25, v/v, eluent), the desired nonapyrrole (**2**) in 73% yield. By carrying out a similar condensation, but employing one molar equivalent each of **8** and **10** (produced from **7** in situ), respectively, the corresponding hexapyrrolic target **4** was obtained in 82% yield (Scheme 2). Finally, by replacing the monoformylterpyrrole **8** by the corresponding bipyrrole **13** (prepared from diester **11**[9c] in analogy to **8**), it proved possible to isolate the heptapyrrin **3** in 45% yield following chromatographic purification (Scheme 3). As detailed in the Experimental Section, satisfactory spectroscopic data was obtained for all three of these new oligopyrroles.

The three new oligopyrroles reported here, namely **2**−**4**, are formally conjugated systems possessing 36 (**2**), 28 (**3**), and 24 (**4**) π-electrons, respectively. As might be expected, therefore, all three compounds are deeply colored, generating violet solutions when dissolved in, for example, dichloromethane. The visible electronic spectra of the free base derivatives of **2** and **3** each contains three bands. These appear at λ_{max}/nm: 330, 527, and 638 nm and 333, 501 and 633 nm in the case of **2** and **3**, respectively (Figures 1 and 2). Both of these spectra are qualitatively similar, with the only difference being that the most intense absorption feature in the spectrum of **2** is the band centered at 527 nm (ϵ/dm^3·mol^{-1}·cm^{-1} = 29 300) whereas that for **3** is at 333 nm (ϵ/dm^3·mol^{-1}·cm^{-1} = 32 300). However, on a more quantitative level, the absorption features of **2** are all seen to be shifted to the red compared to those of **3**. This is consistent with a model wherein the net conjugation in **2** is enhanced relative to that of **3**.

The oligopyrroles **2** and **3** were also characterized spectroscopically in the form of their bis-HOAc adducts

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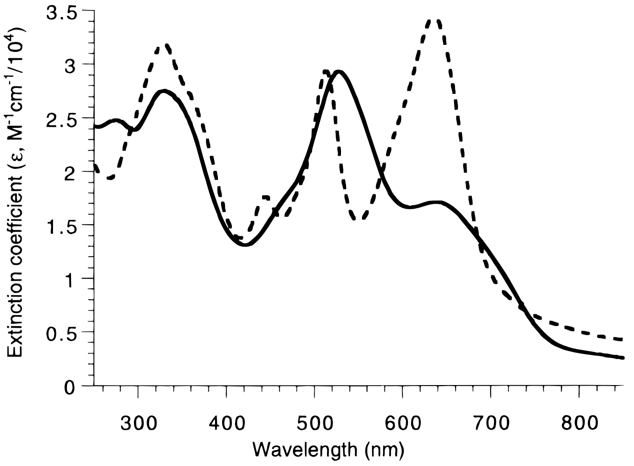


Figure 1. UV/vis absorption spectrum of the nonapyrrole **2** recorded as the free base in dichloromethane (—) and after addition of excess acetic acid (- - -).

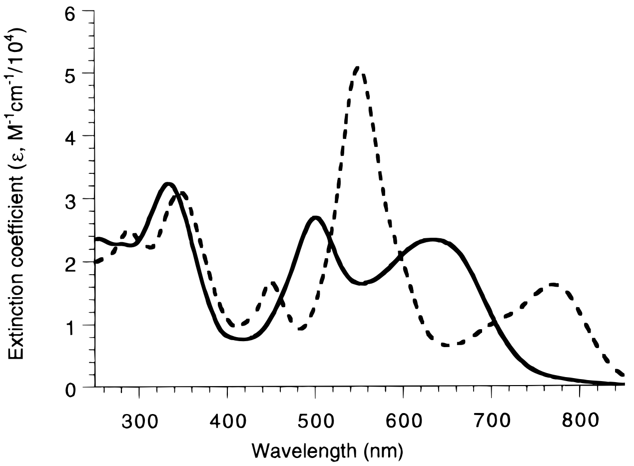


Figure 2. UV/vis absorption spectrum of the heptapyrrole **3** recorded as the free base in dichloromethane (—) and after addition of excess acetic acid (- - -).

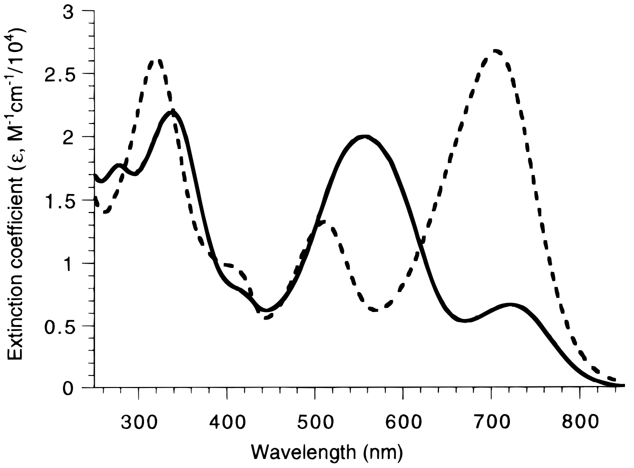


Figure 3. UV/vis absorption spectrum of the hexapyrrole **4** recorded as the free base in dichloromethane (—) and after addition of excess acetic acid (- - -).

(generated in situ by adding excess acetic acid to dichloromethane solutions of the respective free base materials). In both instances diprotonation results in a discernible color change (dichloromethane solutions are now blue (**2**•2HOAC) or pink (**3**•2HOAC), not violet) and in a red-shifting of the lowest energy absorption band (see the Experimental Section for numerical listing of λ_{max} values). Nonetheless, the qualitative finding that the bands of **2** appear to be more red-shifted than those of **3** also appears to hold true in the case of the bis-HOAc adducts.

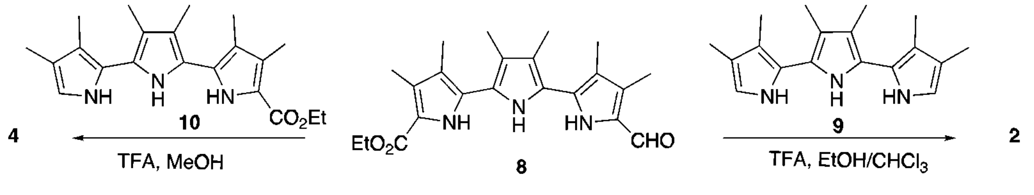
Although an obvious congener from a synthetic perspective, strictly speaking the hexamer **4** is not a direct electronic analogue of **2** and **3**. This is due to the fact that this small system contains only one methine bridge whereas both **2** and **3** possess two sp^2-hybridized carbon linkage units. Nonetheless, as expected, compound **4** does display an electronic spectrum in dichloromethane characteristic of an extended oligopyrrolic system (i.e., λ_{max}/nm = 338 and 557; ϵ/dm^3•mol^{-1}•cm^{-1} = 21 900 and 20 000, respectively) (Figure 3). In this instance, adding excess acetic acid leads to the formation of a monoprotonated adduct. This species is blue-gray in dichloromethane solution and displays absorption maxima at 319, 510, and 705 nm.

In addition to their optical characteristics, the other salient feature of compounds **2**−**4** is their remarkable stability. Indeed, under normal laboratory conditions, none of these species is observed to undergo appreciable degradation over the course of weeks either as solids or as solutions in dichloromethane. The substantial increase in the stability of **2**−**4** with regard to the various 2,5-linked oligopyrroles[5,6] known in the literature is ascribed to the presence of substituents in the α- and β-positions of the pyrrole moieties in **2**−**4**. This stability abetted efforts to obtain single crystals suitable for X-ray diffraction analyses. In the case of **2**, diffraction grade crystals were obtained by allowing hexanes to diffuse into a solution of the free base form in THF. Hexanes diffusion was also used to grow X-ray quality crystals of **4**. Here, however, the initial solution of the free base was made up in dichloromethane. Finally, while attempts have been made to obtain crystals of **3**, so far these efforts have not culminated in success.

The molecular structure of **2**, obtained from the X-ray diffraction analysis, is shown in Figure 4. On a most basic of levels it confirms the structural assignment made for this material. It also reveals other interesting features of this unprecedented system. For instance, it helps illustrate the fact that molecules of **2**, obtained as crystals from THF solution (vide supra), are in hydrogen-bonding contact with 1 of 2 molar equiv of THF found in the solid state. Specifically, N8, a pyrrolic nitrogen in one of the "outer" terpyrrole fragments, is involved in an NH•••O interaction with O1A of a THF molecule.

Two other critical hydrogen-bonding interactions are also seen in the structure of **2**. These involve the ester

Scheme 2



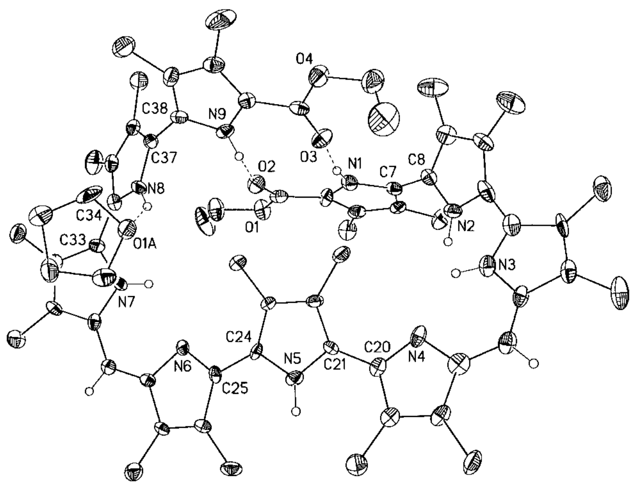
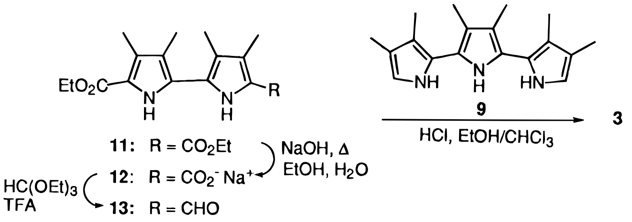


Figure 4. View of $\mathbf{2}\cdot 2(C_4H_8O)$ illustrating the H-bonding interactions (dashed lines), and a partial atom labeling scheme. One molecule of the two THF molecules present in the lattice as solvate (per unit of 2) is hydrogen bound to N8 of the polypyrrole. The other THF molecule is not shown. The polypyrrole forms a loop closed by a set of head-to-tail hydrogen-bonding interactions. Relevant geometries for these interactions are: N1−H1N···O3, N···O 2.92(1) Å, H···O 2.03(1) Å, N−H···O 167(1)°; N9−H9N···O2, N···O 2.79(1) Å, H···O 1.99(1) Å, N−H···O 146.4(9)°; N8−H8N···O1A, N···O 2.92(1) Å, H···O 2.15(1) Å, N−H···O 143.6(9)°. Thermal ellipsoids are scaled to the 30% probability level.

Scheme 3



functions and the NH groups located in the two terminal pyrrole subunits. As a result, presumably, of these interactions, this particular oligopyrrole wraps around itself to form a three-dimensional head-to-tail loop. This looping is, in turn, manifest in terms of a very distinct deviation from a planar molecule conformation. Since only the two terminal pyrroles are involved in these intramolecular hydrogen-bonding interactions, it is perhaps not surprising that the "twist" between these subunits and their nearest pyrrolic "neighbors" is larger than that seen for any other pyrrole−pyrrole pair. Specifically, torsion angles of 105.3(12)° and 60.3(15)° are observed for N1−C7−C8−N2 and N8−C37−C38−N9, respectively. By contrast, the largest other torsion angle observed, that between the pyrroles bearing nitrogens N8 and N7, is −37.0(2)° (i.e., for N7−C33−C34−N8) and can easily be rationalized in terms of the hydrogen bond formed between the THF oxygen atom and the H atom on N8. Furthermore, within the central terpyrrole an almost coplanar geometry is found (torsion angles for N4−C20−C21−N5 and N5−C24−C25−N6 are 166.5(10)° and −173.1(9)°, respectively).

The X-ray analysis of the hexapyrrin **4** free base also reveals some interesting features (Figure 5). Although it possesses a fully conjugated electronic network nature and an exocyclic double bond in the *Z* configuration, in the solid-state compound **4** is not completely planar (Figure 5). Indeed, in **4**, the pyrroles containing nitrogens N1 and N2 are twisted with respect to the four other nearly coplanar pyrroles (the torsion angles for N1−C7−C8−N2 and N2−C11−C12−N3 are 120.5(7)° and −49.3(9)°, respectively). This is due to the fact that N1 and N2 act as hydrogen bond donors to carbonyl groups in other molecules. They thus also help to form a self-assembled polymer in the solid state (Figure 6).

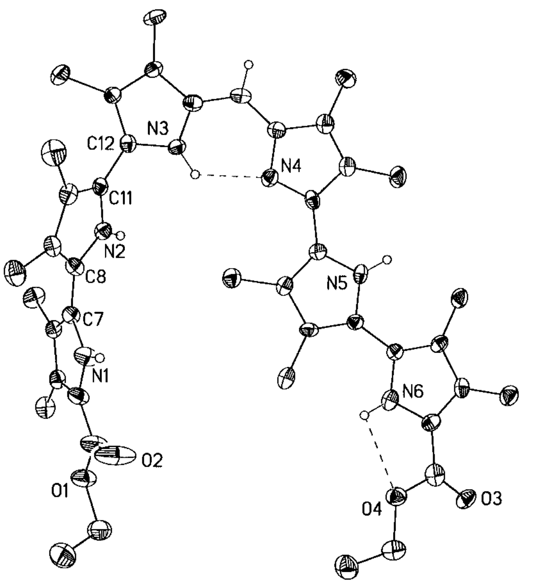


Figure 5. View of **4** with only the oxygen and nitrogen and a few carbon atoms labeled. One terpyrrole (containing N4, N5 and N6), the meso carbon, and the adjacent pyrrole are nearly planar. Thermal ellipsoids are scaled to the 30% probability level. Most hydrogen atoms have been omitted for clarity.

Conclusion

In summary, we have developed a synthetic methodology that appears to be of versatile utility in terms of allowing for the construction of easy-to-isolate oligopyrroles. The resulting materials, characterized by their remarkable stability, could constitute important precursors useful for the construction of novel expanded porphyrins or interesting molecular recognition units in their own right. Consistent with this latter supposition, we have recently found in preliminary work that **4** is able to bind fluoride and chloride anions in a 1:1 fashion and with good affinity in dichloromethane-d_2 solution at 298 K (fluoride, $K_a = (3.46 \pm 0.47) \times 10^3$ M^{-1}; chloride, $K_a = 11.6 \pm 0.8$ M^{-1}). These results, which we are presently exploring further, lead us to suggest that systems such as **2**−**4**, despite (i) being noncationic and (ii) acyclic in nature, could constitute good anion and/or neutral substrate binding agents.

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were measured at 25 °C at 250 and 62.5 MHz, respectively. All coupling constants are measured in hertz (Hz). FAB mass spectra were recorded using nitrobenzyl alcohol (NBA) as the matrix. Methanol was dried by distillation from calcium hydride under a nitrogen atmosphere.

Synthesis. 5,5″-Bis((2-(ethoxycarbonyl)-3,4,3′,4′,3″,4″-hexamethyl-5,2′:5′,2″-terpyrrol-5″-yl)vinyl)-3,4,3′,4′,3″,4″-hexamethyl-2,2′:5′,2″-terpyrrole (2). 2-(Ethoxycarbonyl)-2″-formyl-3,4,3′,4′,3″,4″-hexamethyl-5,2′:5′,5″-terpyrrole (**8**) (81.0 mg; 212 μmol) was dissolved in a 1:1 mixture of $CHCl_3$ and absolute ethanol (40 mL total volume) at rt. The solution was then degassed with argon and the bis α-free terpyrrole **9** (29.8

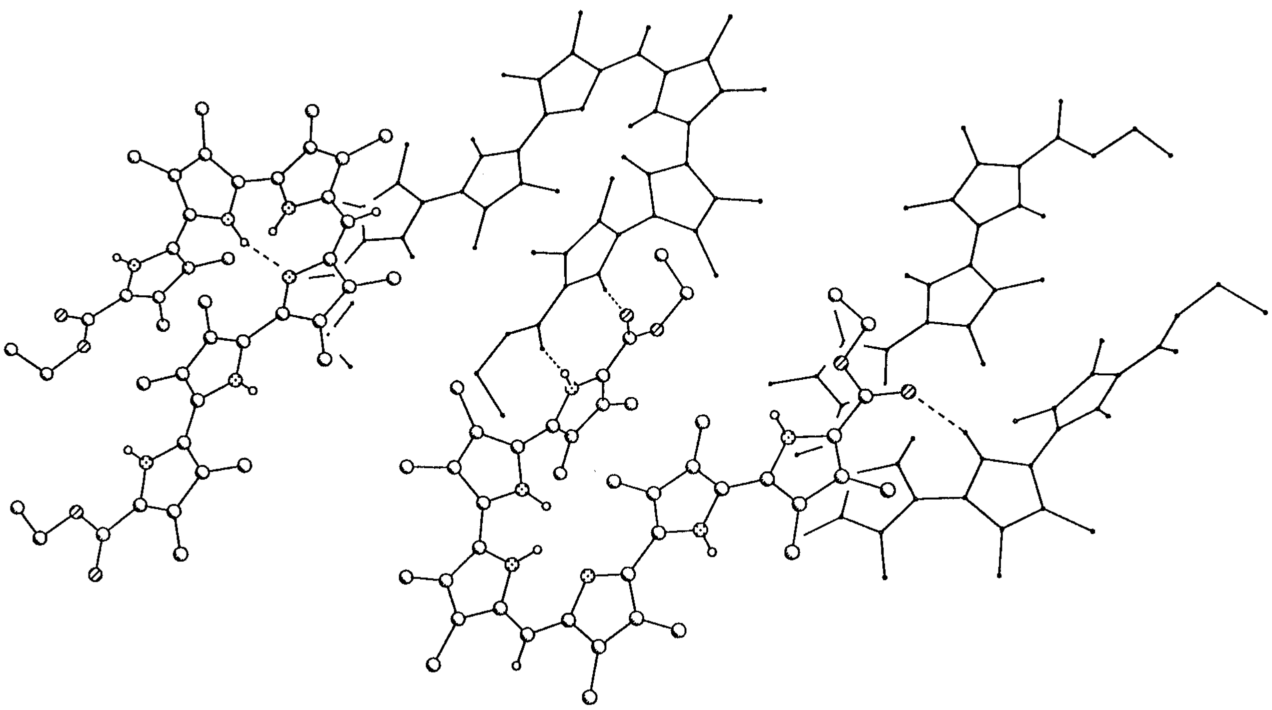


Figure 6. X-ray structure of **4** showing interactions in the solid state. The solid state consists of layers of hydrogen bound molecules. Layers are π-stacked via close contacts between adjacent terpyrrole moieties with plane-to-plane stacking distances of 3.4 Å. Molecules related by a crystallographic inversion center at $^1/_4$, $^1/_4$, $^1/_2$ are connected by two equivalent H-bonds with relevant geometry: N1−H1N···O2 (related by $^1/_2 - x$, $^1/_2 - y$, $1 - z$), N···O 2.807(8) Å, H···O 1.914(8) Å, N−H···O 171.2(6)°. These H-bound dimers are then H-bonded to adjacent dimers related by a crystallographic 2-fold rotation axis with relevant geometry: N2−H2N···O3 (related by $^1/_2 - y$, $^1/_2 + x$, $^1/_2 - z$) N···O 2.995(7) Å, H···O 2.150(7) Å, N−H···O 156.1(6)°. This H-bonding pattern is repeated forming layers of H-bound molecules.

mg; 106 μmol) added along with three drops of TFA. After 48 h solvents were removed on the rotary evaporator and the crude product purified by flash chromatography (column, 25 × 3 cm; silica gel; eluent, 3:1 NH_3-saturated hexanes/CH_2Cl_2). Fractions containing the product were collected and evaporated to dryness. This yielded **2** as a dark violet powder (78.0 mg; 77.4 μmol; 73%): R_f 0.28 (TLC; silica gel; 6:4 NH_3-saturated hexanes/CH_2Cl_2). ^{1}H NMR (DMSO-d_6) δ 11.12 (s, 2H), 10.49 (s, 2H), 10.43 (s, 2H), 8.31 (s, 1H), 6.83 (s, 2H), 4.20 (q, J = 7.0, 4H), 2.24 (s, 6H), 2.17 (s, 24H), 2.13 (s, 12H), 1.97 (s, 12H), 1.27 (t, J = 7.0, 6H); ^{13}C NMR (DMSO-d_6) δ 160.9, 144.9, 144.6, 138.7, 138.4, 133.9, 126.5, 126.2, 125.1, 124.1, 123.9, 123.2, 122.4, 120.2, 118.8, 118.4, 118.0, 113.8, 79.2, 59.0, 14.4, 10.8, 10.6, 10.5, 10.1, 10.0, 9.8, 9.4; HRMS (FAB$^+$) m/z calcd for $C_{62}H_{73}N_9O_4$ 1007.5785, found 1007.5773; UV−vis (CH_2Cl_2) λ_{max} [nm] (ϵ) free base **2** 275 (24 800), 330 (27 500), 527 (29 300), 638 (17 000); **2**·2HOAc 328 (31 900), 444 (17 600), 513 (29 300), 635 (34 300).

5,5″-Bis((2-ethoxycarbonyl-3,4,3′,4′-tetramethyl-5,2′-bipyrrol-5′-yl)vinyl)-3,4,3′,4′,3″,4″-hexamethyl-2,2′:5′,2″-terpyrrole (3). In a three-neck 250 mL round-bottom flask were placed both 2-(ethoxycarbonyl)-2′-formyl-3,3′,4, 4′-tetramethyl-5,5′-bipyrrole (**13**) (0.0482 g; 0.167 mmol) and absolute ethanol (6 mL). Chloroform (150 mL) was added with the bis-α-free terpyrrole **9** (0.0235 g; 0.083 mmol). Concd HCl (2 drops) was added, and the dark violet reaction mixture was stirred at rt under an argon atmosphere for 4 h. The solvent was removed using a rotary evaporator and the product purified by column chromatography (silica gel; eluent, hexanes/EtOAc, 8/2) to give, after removal of eluting solvent, compound **3** as a dark violet solid (62 mg; 45%): ^{1}H NMR (CD_2Cl_2) δ 9.59 (br, 3H), 9.13 (br, 2H), 6.80 (s, 2H), 4.26 (q, J = 7.0, 4H), 2.29 (t, J = 7.7, 9H), 2.21 (s, 9H), 2.08 (s, 12H), 2.04 (s, 12H), 1.33 (t, J = 7.0, 6H); ^{13}C NMR (CD_2Cl_2) δ 177.3, 161.5, 150.3, 142.9, 133.3, 132.4, 129.8, 129.4, 128.1, 127.7, 126.7, 126.5, 126.0, 124.0, 123.3, 123.1, 120.6, 120.4, 120.2, 119.9, 115.1, 60.5, 60.3, 14.7, 11. 9, 10.8, 10.5, 10.3, 9.9, 9.8, 9.0; HRMS (CI$^+$) m/z calcd for $C_{50}H_{59}N_7O_4$ 821.4628, found 821.4632; UV−vis (CH_2Cl_2) λ_{max} [nm] (ϵ) free base **3** 333 (32 300), 500 (26 900), 633 (23 300); **3**·2HOAc 289 (25 000), 347 (30 900), 450 (16 700), 550 (50 600), 771 (16 100).

Bis(2-(ethoxycarbonyl)-3,4,3′,4′,3″,4″-hexamethyl-5,2′:5′,2″-terpyrrol-5″-yl)methene (4). The terpyrrole monosodium salt **7** (119 mg; 283 μmol) and monoformyl terpyrrole **8** (108 mg; 283 μmol) were suspended together in anhydrous methanol (40 mL) and the resulting mixture degassed with argon. The suspension was then heated to 40 °C, and TFA (44 μL; 566 μmol) was added under an argon atmosphere. After all of the starting materials were dissolved, the reaction mixture was allowed to cool to rt prior to stirring for an additional 24 h. The reaction mixture was then taken to near dryness under reduced pressure and the resulting dark-green residue purified by flash chromatography (column 25 × 3 cm; silica gel; eluent, 3:1 NH_3-saturated hexanes/CH_2Cl_2). Fractions containing the product **4** were collected and evaporated to dryness. This gave target **4** as a dark violet powder (166 mg; 232 μmol; 82%): R_f 0.25 (TLC; silica gel; 7:3 NH_3-saturated hexanes/EtOAc); ^{1}H NMR (benzene-d_6) δ 12.50 (br, s, 2H), 10.64 (br, s, 1H), 10.58 (br, s, 2H), 6.58 (s, 1H), 4.13 (q, J = 7.1, 4H), 2.10 (s, 6H), 2.01 (s, 12H), 1.99 (s, 6H), 1.83 (s, 6H), 1.81 (s, 6H), 1.05 (t, J = 7.1, 6H); ^{13}C NMR (benzene-d_6) δ 161.9, 145.4, 139.7, 134.8, 126.3, 124.6, 123.9, 122.4, 120.7, 119.8, 119.5, 118.9, 114.2, 77.6, 59.9, 14.5, 11.6, 11.2, 10.9, 10.2, 10.0, 9.7; HRMS (CI$^+$) m/z calcd for $C_{43}H_{53}N_6O_4$ 717.4128, found 717.4114; UV−vis (CH_2Cl_2) λ_{max} [nm] (ϵ) free base **4** 278 (17 700), 338 (21 900), 557 (20 000), 721 (6600); **4**·HOAc 319 (26 300), 510 (13 200), 705 (26 700).

Sodium 2″-(Ethoxycarbonyl)-3,4,3′,4′,3″,4″-hexamethyl-5,2′:5′,2″-terpyrrole-2-carboxylate (7). 2,5-Bis(3,4-dimethyl-2-ethoxycarbonyl-5-pyrryl)-3,4-dimethylpyrrole (**6**) (2.09 g; 4.91 mmol) was dissolved in p-dioxane (25 mL) and the solution heated to 80 °C. An aqueous NaOH solution (1 M; 7.86 mL) was added at once and the reaction mixture stirred at 80 °C for 4.5 h. The solvents were evaporated, and the brown residue was purified by flash chromatography (column, 20 × 5 cm; silica gel; eluent, 85/15/2 CH_2Cl_2/MeOH/25% aqueous NH_4OH). This yielded the terpyrrole monoacid **7** as a greenish solid (600 mg; 1.43 mmol; 29%): R_f 0.5 (TLC; silica gel; 95:5:1

CH_2Cl_2/MeOH/HOAc); ^{1}H NMR (DMSO-d_6) δ 10.86 (br, 1H), 10.70 (br, 1H), 10.42 (br, 1H), 4.21 (q, $J = 7.1$, 2H), 2.21 (s, 6H), 2.20 (s, 6H), 1.93 (s, 6H), 1.26 (t, $J = 7.0$, 3H); ^{13}C NMR (DMSO-d_6) δ 162.4, 160.9, 127.0, 126.4, 126.2, 125.9, 120.6, 120.3, 118.3, 117.6, 117.2, 117.1, 116.8, 116.6, 58.9, 14.5, 10.6, 10.4, 10.0, 9.3; HRMS (FAB$^-$) m/z calcd for $C_{22}H_{26}N_3O_4$ 396.1923, found 396.1917.

2-(Ethoxycarbonyl)-2″-formyl-3,4,3′,4′,3″,4″-hexamethyl-5,2′:5′,5″-terpyrrole (8). To a degassed mixture of triethyl orthoformate (10 mL) and TFA (15 mL) held at −5 °C was added the terpyrrole monosodium salt **7** prepared as above (340 mg; 811 μmol), and the resulting solution was stirred at this temperature for 1.5 h. The reaction mixture was quenched by adding cold water (40 mL) and the suspension extracted with $CHCl_3$ (3 × 20 mL). The organic phase was washed with 1 N aqueous NaOH solution (30 mL). It was then dried (Na_2SO_4) and taken to near-dryness under reduced pressure. The resulting residue was purified by flash chromatography (column, 25 × 3 cm; silica gel; eluent, 8:2 hexanes/EtOAc or neat $CHCl_3$). After evaporative removal of eluting solvents, this afforded **8** (201 mg; 527 μmol; 65%): R_f 0.24 (7:3 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$) δ 9.61 (s, 1H), 9.13 (br, s, 1H), 8.90 (br, s, 1H), 4.32 (q, $J = 7.2$, 2H), 2.31 (s, 6H), 2.16 (s, 3H), 2.14 (s, 3H), 2.12 (s, 3H), 2.11 (s, 3H), 1.33 (t, J = 7.1, 3H); ^{13}C NMR ($CDCl_3$) δ 176.4, 161.8, 133.7, 131.6, 128.9, 127.7, 125.8, 122.1, 120.4, 119.7, 118.9, 118.8, 118.7, 118.5, 14.5, 10.8, 10.6, 10.3, 10.2, 8.9; HRMS (CI$^+$) m/z calcd for $C_{22}H_{27}N_3O_3$ 381.2052, found 381.2048.

Sodium 2′-(Ethoxycarbonyl)-3,4,3′,4′-tetramethyl-5,5′-bipyrrole-2-carboxylate (12). Diethyl 3,4,3′,4′-tetramethyl-5,5′-bipyrrole-2,2′-dicarboxylate (**11**) (27.51 g; 82.76 mmol) was placed in a 2 L three-neck round-bottom flask with absolute ethanol (1.5 L). Then an aqueous NaOH solution (3.3 g in 150 mL H_2O) was added and the reaction mixture heated under reflux for 24 h. The solvent was then removed in vacuo and the resulting pink solid washed several times with distilled water and chloroform until no remaining starting material **11** could be detected by TLC analysis. Compound **12** was obtained as a pink solid (12.4 g; 46%): ^{1}H NMR (DMSO-d_6) δ 11.12 (br, 1H), 10.29 (br, 1H), 4.16 (q, $J = 7.1$, 2H), 2.20 (s, 3H), 2.16 (s, 3H), 1.85 (s, 3H), 1.83 (s, 3H), 1.25 (t, $J = 7.1$, 3H); ^{13}C NMR (DMSO-d_6) δ 167.6, 160.9, 126.9, 126.0, 120.4, 119.4, 117.7, 117.4, 116.9, 58.8, 14.3, 10.4, 10.2, 10.1, 9.9; HRMS (CI$^+$) m/z calcd for $C_{16}H_{20}N_2O_4$ 304.1423, found 304.1426.

2-(Ethoxycarbonyl)-2′-formyl-3,4,3′,4′-tetramethyl-5,5′-bipyrrole (13). Under an argon atmosphere, sodium 2′-(ethoxycarbonyl)-3,4,3′,4′-tetramethyl-5,5′-bipyrrole-2-carboxylate (**12**) (22.10 g; 67.72 mmol) was placed in a 2 L, three-neck round-bottom flask previously cooled in an ice/water bath. TFA (260 mL) was then added and the resulting dark brown solution stirred in the ice/water bath for 30 min. Anhydrous triethyl orthoformate (260 mL) was added while the reaction was still being cooled. The resulting dark green solution was stirred for an additional 3 h in the ice/water bath. Water (1 L) was then added, giving a blue solid. This solid was extracted with CH_2Cl_2, and the blue organic layers so obtained were washed once with a 1 N aqueous NaOH solution and with brine before being dried over Na_2SO_4. After the solvent was removed, compound **13** was obtained as a violet solid (9.4 g; 48%): ^{1}H NMR (DMSO-d_6) δ 11.58 (br, 1H), 11.33 (br, 1H), 9.59 (s, 1H), 4.22 (q, $J = 7.1$, 2H), 2.25 (s, 3H), 2.22 (s, 3H), 1.88 (s, 6H), 1.27 (t, $J = 7.1$, 3H); ^{13}C NMR (DMSO-d_6) δ 177.5, 160.8, 129.1, 128.7, 126.0, 124.6, 119.5, 119.1, 119.0, 59.2, 14.4, 10.5, 9.8, 9.5, 9.0; HRMS (FAB$^+$) m/z calcd for $C_{16}H_{21}N_2O_3$ 289.1552, found 289.1544.

X-ray Diffraction Analysis. Crystals of **2**·2(C_4H_8O) grew as dark prisms by diffusion of hexanes into a THF solution of **2**. The data crystal was of approximate dimensions 0.15 × 0.27 × 0.31 mm. Crystals were triclinic, space group $P\bar{1}$, with $a = 12.642(6)$ Å, $b = 14.456(10)$ Å, $c = 18.907(8)$ Å, $\alpha = 82.45(5)°$, $\beta = 90.73(1)°$, $\gamma = 83.16(4)°$, $V = 3235(3)$ Å^3, $\rho_{calc} = 1.18$ g·cm^{-3} for $Z = 2$. Data were collected at −85 °C on a Siemens P4 diffractometer, equipped with a Nicolet LT-2 low-temperature device and using a graphite monochromator with Mo Kα radiation ($\lambda = 0.71073$ Å). Diffraction peaks were quite broad, and therefore, a scan range of 2.0° ω was employed. The broad diffraction peaks and poor scattering ability of the crystal contributed to the high values for R_{int}, $R(F_o)$, and $R_w(F_o^2)$. The structure was solved and refined using the Shelxtl-*Plus* (Siemens Analytical X-ray Instruments, Inc., Madison, WI) software package. The structure was refined on F^2 to a $R_w = 0.255$ using 8387 unique reflections and 758 parameters (conventional $R(F) = 0.114$ for 3037 reflections with $F > 4(\sigma(F))$. Full details of the structure determination, along with tables of atomic coordinates, bond lengths and angles, and thermal parameters, as well as supplementary figures, are given in the Supporting Information.

Crystals of **4**·1/2C_6H_{14} grew as very dark, almost black prisms by vapor diffusion of hexanes into a CH_2Cl_2 solution of **4**. Crystals were monoclinic, space group $C2/c$ with $a = 15.732(2)$ Å, $b = 20.263(3)$ Å, $c = 26.252(5)$ Å, $\beta = 90.73(1)°$, $V = 8368(2)$ Å^3, $\rho_{calc} = 1.21$ g·cm^{-3} for $Z = 8$. Data were collected using the ω scan technique to 50° in 2θ at −90 °C on a Siemens P3 diffractometer (Mo Kα radiation, $\lambda = 0.71073$ Å). The structure was solved and refined using the Shelxtl-*Plus* (Siemens Analytical X-ray Instruments, Inc., Madison, WI) software package. The structure was refined on F^2 to a $R_w = 0.190$ using 7375 unique reflections and 510 parameters (conventional $R(F) = 0.104$ for 2570 reflections with $F > 4(\sigma(F))$. Full details of the structure determination, along with tables of atomic coordinates, bond lengths and angles, and thermal parameters, as well as supplementary figures, are given in the Supporting Information.

Binding Constant Determinations. Anions were added in the form of a 1.12 M CD_2Cl_2 anhydrous tetrabutylammonium salt solution for chloride and a 0.140 M CD_2Cl_2 trihydrate tetrabutylammonium salt solution for fluoride anion to 7 mM solutions of the receptor in CD_2Cl_2 with the concentration changes being accounted for by EQNMR.[14] In determining the stability constants and in deducing the proposed 1:1 binding stoichiometry, the possible effects of ion pairing (if any) were ignored. Also ignored were the potential effects of the three water molecules of crystallization present in the fluoride anion solutions employed for the titrations.

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Supporting Information Available: X-ray structural data for **2** and **4**, including X-ray experimental, summaries crystallographic parameters, atomic coordinates, bond distances and angles, and anisotropic thermal parameters, and HPLC traces and high-resolution mass spectrometric data for compounds **2**, **3**, **4**, **7**, **8**, and **13** (61 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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